REMARKS

Claims 1-7, 28, 85-87, 104, 107-109, 116, 117, 123, 130, 131 and 138-148 are pending in the application. Claims 1, 2, 85 and 139-148 are currently amended. Claims 8-27, 29-84, 88-103, 105, 106, 110-115, 118-122, 124-129 and 132-137 are cancelled herein, without prejudice.

By this Office Action, the Examiner has required restriction to one of the following inventions under 35 U.S.C. §121:

I. Claims 1-7 and 28, drawn to a method of increasing splice site selection by hybridizing an oligonucleotide-protein conjugate to a target pre-mRNA molecule in a cell.

II. Claims 1-7 and 28, drawn to a method of repressing splice site selection.

III. Claims 85-87, 138 and 148, drawn to an oligonucleotide for modulating splice site.

IV. Claims 104 and 140, drawn to a method of creating an alternate form of mRNA.

IV. Claims 107-108, 141-142 and 147, drawn to a method of inhibiting mRNA expression or neuronal differentiation comprising administering an oligonucleotide for modulating splice site.

V. Claims 109, 116-117, 123, 130-131 and 144-146, drawn to methods of treating or preventing diseases.

In response to the Restriction Requirement mailed September 26, 2007, Applicants provisionally elect, with traverse, to prosecute the claims of Group I, namely claims 1-7 and 28, drawn to a method of modulating splice site selection and splicing thereof, said method comprising the step of hybridizing an oligonucleotide to a target pre-mRNA molecule in a cell.

Applicants however respectfully disagree that Groups I to VI do not relate to a single general inventive concept, in view of Astriab, Fisher et al. Astriab, Fisher et al. describe a peptide-oligonucleotide conjugate, wherein a peptide is covalently linked to the oligonucleotide in order to enhance the oligonucleotide delivery to the nucleus, to facilitate transport of the oligonucleotide into the cell.

Claim 1 has been amended to more clearly define the claimed invention. Specifically, the expression "oligonucleotide-protein conjugate" has been replaced with the word "oligonucleotide". Support can be found throughout the specification that this oligonucleotide-protein conjugate is indeed an oligonucleotide.

Furthermore, claims 1, 85 and 139-148 have been amended to remove the word "covalently". Support can be found throughout the specification and more particularly on pages 15 (2nd full paragraph), 24 (2nd full paragraph), and 26 (2nd full paragraph) and in the Examples, such as Example 1. In claims 139-148, the word "attached" has been replaced with the word "bound".

It is therefore submitted that:

- amended claim 1 is not described or taught by Astriab, Fisher et al.;
- the inventions of Groups I to VI share special technical features that define a contribution over the prior art of Astriab, Fisher et al., namely methods of modulating splice site selection and splicing thereof comprising an oligonucleotide and a protein moiety which are not covalently linked, and oligonucleotides thereof; and that
- in contrast to Astriab, Fisher et al., in the present invention, the protein is not recruited before entering the cell, but once inside the cell.

According to the MPEP, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

The inventions must be independent (see MPEP # 802.01, # 806.04, #808,01), or distinct as claimed (see MPEP w 806.05 – w 806.05(i)); and

There must be a serious burden on the Examiner if restriction is not required (see MPEP w 803.02, # 806.04(a)-(j), # 808.01(a) and # 808.02).

It is believed that the inventions, as defined in claims 1-7, 28, 85-87, 104, 107-109, 116, 117, 123, 130, 131 and 138-148, are not independent, as Group III is directed to an oligonucleotide modulating the splice site used in Group I to increase said splice site selection, in

Group II to decrease said splice site selection, in Group IV to create an alternate form of mRNA (by modulating the splice site, the mRNA will be different), in Group V to inhibit mRNA expression or neuronal differentiation (by modulating the splice site, the mRNA expression or neuronal differentiation will be different) and in Group VI to treat or prevent diseases due to alternate splicing.

It is believed that it would not cause a serious burden on the Examiner to search and examine all pending claims because all claims involve methods and compounds comprising the same oligonucleotide of the invention.

Therefore, the requirements of MPEP of §803 are not met.

Withdrawal of the Restriction Requirement and examination of claims 1-7, 28, 85-87, 104, 107-109, 116, 117, 123, 130, 131 and 138-148 on the merits are respectfully requested.

The instant oligonucleotide sequences are alleged to be separate inventions. Applicants elect with traverse SEQ ID NO:12. Applicants respectfully disagree as it is submitted that the oligonucleotide sequences share a conserved part, *i.e.* structure, that binds to the protein moiety and a conserved function, i.e. modulating splice site selection and splicing thereof.

This is a complete response to the requirement for restriction mailed on September 26, 2007.

Applicants submit concurrently herein a petition for extension of time to and including December 26, 2007, accompanied by the required fee.

No new matter has been added by the present amendment. Applicant respectfully submits that the present amendment does not raise any new issue under 35 USC 112.

It is believed that the present claims are in condition for allowance. Prompt and favorable consideration is earnestly solicited.

In the event that there are any questions concerning this Amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

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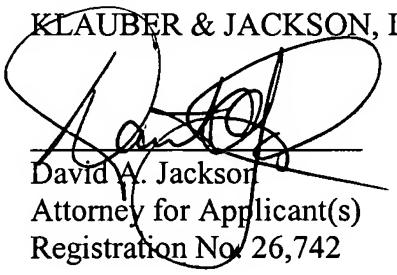

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